

Menstrual-like vaginal bleeding in prepubertal girls: an unexplained condition

M. MERCKX¹, S. WEYERS², R. SANTEGOEDS³, J. DE SCHEPPER⁴

¹ Division of Pediatric Gynaecology, University Hospital St Pieter and Erasmus Brussels & ICRH Ghent Belgium.

² Department of Obstetrics and Gynaecology, Ghent University Hospital & ICRH Ghent Belgium.

³ Medical Master student, KUL Leuven Belgium.

⁴ Division of Pediatric Endocrinology, Department of Pediatrics, University Hospital Brussels and Ghent University Hospital Belgium.

Correspondence at: mireillemerckx@gmail.com

Abstract

Unexplained menstrual-like cyclic vaginal bleeding, lasting for several days and without any uterine and vaginal anomaly, is a rare condition in prepubertal girls. Only small series (containing four to eleven cases) have been described in literature. We report our in nine girls presenting with vaginal bleeding without any abnormality at gynaecological, hormonal and echographic examination.

Key words: Prepubertal vaginal bleeding, menarche, telarche, isolated menses, environment.

Introduction

Recurrent vaginal bleeding is a rare symptom in prepubertal girls. When the vaginal bleeding is cyclic and lasts for two to five days, isolated menses should be considered. The first menstruation normally appears approximately two and a half years after the onset of breast development. The occurrence of a menstrual-like bleeding before telarche is very rare and has also been defined as premature menarche analogous to premature pubarche and premature telarche. These conditions are considered as an incomplete form of precocious puberty since no other signs of puberty are present.

The pathophysiology of cyclic vaginal bleeding in prepubertal girls is not well understood and is thought to be due to unusual sensitivity of the endometrium to very low prepubertal levels of oestrogens (Stanhope, 2006; Traggiai *et al.*, 2003). In one study a seasonal effect was suspected (Blanco *et al.*, 1985). It is possible that a range of environmental factors can influence the prepubertal endometrium and thus be involved in abnormal

bleeding patterns (Croes *et al.*, 2009; Degen *et al.*, 2004; Mouritsen *et al.*, 2010; Munro *et al.*, 2010; Nebesio *et al.*, 2005).

We report on nine girls who presented with menstrual-like cyclic vaginal bleeding during the last three years.

Materials and Methods

From a retrospective case review in four Medical Centers (St Pieter Hospital Brussels, ULB Erasmus Hospital Brussels, Queen Paola's Children Hospital Antwerp and UZ Brussels) we retrieved nine girls with a diagnosis of menstrual-like unexplained vaginal bleeding over a period of three years (between 2009 and 2011).

In all girls a complete clinical examination, including body height, body weight and Tanner staging was performed. Bone age was determined by X-ray of the left hand and wrist, according to the Greulich and Pyle atlas.

Basal concentrations of LH, FSH, E2, DHEAS, progesterone, 17-OH-progesterone, IGF1, PRL, TSH,

Table 1. — Symptomatology and clinical findings.

Patient number	1 st bleeding month	Age at 1 st bleeding (yr)	N° of bleeding events	Duration (N° days)	Ethnic origin	BMI (kg/m ²)	Vulva	Pub. Status (Tanner)
1	April	7	2	< 2	Burkina Faso	14,8	Infantile	A1P1M2
2	May	3	3	< 2	Sierra Leone	14,9	Infantile	A1P1M1
3	October	8	2	< 3	Morocco	20,7	Infantile	A1P1M1
4	November	8	1	4	Belgium	21,3	Infantile	A2P1M2
5	August	4	8	2-3	Turkey	17,2	Infantile	A1P1M1
6	September	7	2	5	Congo	17,1	Infantile	A1P1M1
7	August	7 ½	1	2	Belgium	18,1	Infantile	A1P1M1
8	September	7	2	< 3	Turkey	16,9	Infantile	A1P1M1
9	December	3 ½	2	< 2	Guinea	15,0	Infantile	A1P1M1

T4 were measured. In all patients a GnRH stimulation test (2.5 micrograms/kg bodyweight) was performed (Cesario *et al.*, 2007; Perry *et al.*, 2008). Uterine length, thickness of the endometrial lining, uterine artery flow and ovarian volumes were measured by ultrasound (Badouraki *et al.*, 2008; Munro *et al.*, 2010; Zierissen *et al.*, 2001).

Results

Table 1 and 2 give an overview of the findings in our nine patients.

The included patients were from different ethnic origins and their chronological age at examination ranged from three to ten and a half years. The number of menstrual-like vaginal bleedings varied from one to eight. The duration of bleeding varied from one to five days and in most patients less than three pads were used. No seasonal pattern was evident. Only one girl showed vaginal bleeding at the moment of gynaecological examination. None of the girls had breast development. The vulvar aspect was

normal for their age. One girl showed a café-au-lait spot. Growth data, including the BMI, were normal (Rosenfeld *et al.*, 2009). Bone age was not significantly different from normal. Pelvic ultrasound showed a normal prepubertal sized uterus without endometrial proliferation and with a prepubertal uterine artery flow, with the exception of one girl who had an endometrial lining of 3 mm. Two girls with more than two episodes of vaginal bleeding underwent a vaginotomy but no anomaly was seen. Serum concentrations of oestradiol (< 20 pg/ml), LH (< 1 mIU/ml) and FSH (< 5 mIU/ml) were all within the prepubertal ranges. The peak LH response at GnRH testing was lower than 4.5 mIU/L, which also corresponds to a prepubertal state. None of the girls had clinical or hormonal signs of an exaggerated adrenarche.

Discussion

There are rather scarce data in the literature on prepubertal menstrual-like bleeding (Berberoğlu *et al.*,

Table 2. — Investigations.

Patient number	Bone Age (yr)	LH (mIU/ml)	FSH (mIU/ml)	Oestradiol (pg/ml)	DHEAS (ng/ml)	Peak LH at GnRH (mIU/ml)	Ultrasound Max. uterine length (cm)
1	7	< 0,1	0,9	< 5	230	< 4,5	3,6
2	3	0,5	1,6	10	150	3	2,9
3	8	< 1	3	10	664	2	3,4
4	9	< 0,2	1,3	< 20	312	< 2	3,6
5	4	< 1	1,2	7	250	1,7	1,3
6	7 ½	< 1	< 1	12	230	< 2	2,6
7	8	< 0,2	1,6	6	297	2	3,3
8	7	< 1	3	< 10	604	3	3,4
9	4	< 1	1,6	10	170	< 1	1,5

2009; Heller *et al.*, 1979; Hill *et al.*, 1989; Murram *et al.*, 1983; Shanthi *et al.* 2006). Although a seasonal pattern was found in one study (Blanco *et al.*, 1985), the occurrence of cyclic vaginal bleeding was not related to a specific season in our case. Exclusion of any other underlying pathology is essential and needs the consideration of several underlying conditions. Whether recurrent cyclic prepubertal vaginal bleeding can be defined as prepubertal menarche (Shanthi *et al.*, 2006) or premature menarche (Murram *et al.*, 1983) can be a matter of debate. It could be argued that by definition menarche is one step in the chain of pubertal events and necessitates a certain level of cyclic hormonal changes, which is not the case in this study. Anyway, in all cases reported there was no impact on the subsequent menstrual pattern and fertility prognosis (Sterling, 2007).

Early menarche (before the age of ten years) can occur in case of central precocious puberty. This disorder is by definition gonadotrophin dependent and is caused by a precocious maturation of the hypothalamic pituitary axis, which results in physical and hormonal changes (Cesario *et al.*, 2007). In none of our tested girls a pubertal response to GnRH was seen and no other signs of pubertal development were present.

The response to GnRH test was suppressed (no increase in basal gonadotrophins) in two cases, but this was not associated with an elevated oestradiol level. This might be due to a previous and transient follicular cyst although these transient ovarian cysts are often associated with breast development which was not the case in our patients. A suppressed response of gonadotrophins is seen in other causes of peripheral precocious puberty such as adrenal and ovary tumors. DHEAS values were normal in all our patients and none of them had an advanced bone age, which is classically seen in such cases of peripheral precocious puberty. Two girls were younger than four years of age. In case of uterine bleeding at a very young age (most often below the age of two) McCune Albright syndrome must be considered. This sporadic disorder is accompanied by café-au-lait spots and fibrous bone dysplasia. This triad can also fit into other endocrine pathologies like pituitary adenoma, hyperthyroidism. The ultrasound examination of these children typically shows voluminous ovarian cysts, which was not seen in our cases. Detailed history did not evoke any exposure to exogenous oestrogens in our patients. None of them had taken any herbal medicines or was having contact with a mother, grandmother or caretaker treated with dermal oestrogens.

A temporary activation of the hypothalamic pituitary axis was unlikely in our population of girls with menstrual-like vaginal bleeding, since there was

neither an increase of gonadotrophins nor of oestradiol levels. Ultrasound showed a normal prepubertal state of uterine maturation and the absence of endometrial proliferation. In only one girl endometrial lining was evidenced, suggestive of an increased sensitivity of the endometrium as possible mechanism in this particular case.

Surprisingly, active bleeding was seen in only one girl in our study. We cannot exclude that some of these girls might suffer from the Munchausen by Proxy syndrome. This psychiatric syndrome due to relational problems confirms the importance of an objective evaluation of the vaginal bleeding (Sterling, 2007). Some conditions and symptoms may be faked by the caregiver or the parents and even the child may inflict injury on itself to draw attention and sympathy.

Prepubertal vaginal bleeding is a source of anxiety not only for the girl, but also for her family. In each case a prompt evaluation is recommended and warranted. If no explanation can be found, only clinical observation and reassurance of the girl and parents are necessary (Golub *et al.*, 2008; Posnet *et al.*, 2006). The clinician should also be sensitive to the unspoken concern of possible sexual molestation. Harmful traditional practices of genital mutilation in foreign girls can be another cause of genital bleeding.

Conclusion

The aetiology of cyclic vaginal bleeding in prepubertal girls remains unknown in most cases. It must be differentiated from early pubertal timing and peripheral precocious puberty. More research is needed to clarify its pathophysiology.

References

- Badouraki A, Christoforidis A, Economou I *et al.* Evaluation of pelvic ultrasonography in the diagnosis and differentiation of various forms of sexual precocity in girls. *Ultrasound Obstet Gynecol.* 2008;32(6):819-27.
- Berberoglu M. Precocious Puberty and Normal Variant Puberty: Definition, etiology, diagnosis and current management. *J Clin Res Pediatr Endocrinol.* 2009;1(4):164-74.
- Cesario SK, Hughes LA. Precocious puberty: a comprehensive review of literature, *JOGNN.* 2007;16(3):263-70.
- Croes K, Baeyens W, Bruckers L *et al.* Hormone levels and sexual development in Flemish adolescents residing in areas differing in pollution pressure. *Int J Hyg Environ Health.* 2009;212: 612-25.
- Degen GH, Bolt HM. Endocrine disruptors: update on xenoestrogens. *Int Arch Occup Environ Health.* 2000;73:433-41.
- Golub MS, Collman GW, Toppari J *et al.* Public Health Implications of Altered Puberty Timing. *Pediatrics* 2008;121(3): 218-230.
- Heller ME, Dewhurst J, Grant DB. Premature menarche without other evidence of precocious puberty. *Arch Dis Child.* 1979;54:472-5.

- Hill W, Oppenheimer L, Morton K. The ethiology of vaginal bleeding in children. A 20-year review. *BJOG*. 1989;96(4):467-70.
- Mouritsen A, Aksglaede L, Sørensen K *et al*. Hypothesis: exposure to endocrine-disrupting chemicals may interfere with timing of puberty. *Int J Androl*. 2010;33(2):346-59.
- Munro SK, Farquhar CM, Mitchell MD *et al*. Epigenetic regulation of endometrium during the menstrual cycle. *Mol Hum Reprod*. 2010;16(5):297-310.
- Murram D, Dewhurst J, Grant DB. Short reports Premature menarche: a follow-up study. *Arch Dis Child*. 1983;58:142-56.
- Nebesio T, Pescovitz O. Historical perspectives: endocrine disruptors and the timing of puberty. *Endocrinologist*. 2005;15(1):44-8.
- Posner R. Early Menarche: A Review of Research on Trends in Timing, Racial Differences, Etiology and Psychosocial Consequences. *Sex Roles*. 2006;54:315-22.
- Rosenfeld R, Lipton R, Drum M. Telarche, pubarche and menarche attainment in children with normal and elevated body mass index. *Pediatrics*. 2009;123(1):84-8.
- Shanthi M, Pinto SM, Garden AS. Prepubertal menarche: a defined clinical entity. *Am J Obstet Gyn*. 2006;195(1):327-9.
- Stanhope R. Disorders of puberty. *Medicine*. 2006;37(6):494-6.
- Sterling J Jr. Beyond Munchausen by proxy. *Pediatrics*. 2007;119(5):1026-30.
- Traggiai C, Stanhope R. Disorders of pubertal development. *Best Pract & Res Clin Obstet & Gynaecol*. 2003;17(1):41-56.
- Ziereisen F, Heinrichs C, Avni EF *et al*. The role of doppler evaluation of the uterine artery in girls around puberty. *Pediatr Radiol*. 2001;31:712-9.